REMARKS

Claims 47-56, 58-61 and 63 are currently pending.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 47-56, 58-61 and 63 were rejected under 35 U.S.C. § 112, first paragraph, as not enabled. Specifically, the Examiner asserts that the claims are not enabled because they are drawn to *in vivo* or *ex vivo* delivery of DNA and therefore encompass gene therapy. Applicants respectfully traverse.

Independent claim 47 recites a method for introducing a heterologous gene into a target cell comprising introducing a first and second DNA sequence into a cell of a subject. Independent claim 51 recites a producer cell which comprises a first and second DNA sequence. Independent claim 59 recites a method for making a producer cell comprising introducing a first and second DNA sequence into a cell. Although the claims may encompass gene therapy, they do not recite gene therapy. In particular, the claims do not require a therapeutic effect.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. A patent may be enabling even though some experimentation is necessary, so long as the amount of experimentation is not "undue". See *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991); and *United States v. Telectronics, Inc.* 857 F.2d 778 (Fed. Cir. 1988).

From the teachings in the application, one of skill in the art would be able to introduce a heterologous gene of interest into a target cell of interest using the claimed method. Additionally, the disclosure for the present invention describes a number of delivery methods. The examples also describe delivery methods and producer systems. One of skill in the art, in combinations with the teachings in the disclosure, could readily devise a suitable method for introducing a DNA sequence encoding a defective retroviral genome and DNA sequences encoding packaging components *env* and *gag-pol* into a cell. Applicants therefore request withdrawal of this rejection.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 60, 61 and 63 were rejected under 35 U.S.C. § 112, second paragraph as indefinite. Specifically, claims 60 and 61 were rejected as depending from a cancelled claim. Applicants submit that the amendments to claims 60 and 61, in which the claims have been amended to depend from claim 51, overcomes the rejection with respect to these claims. Applicants traverse this rejection as it is applied to claim 63 and the term "fresh."

The term "fresh" is defined in the specification in the paragraph starting at page 5, line 36 and extending to page 6, line 6. As defined in the specification, the term "fresh" refers to cells that are in their natural state, or as close as possible to their natural state. Cells that have been "extensively cultured *in vitro*, including cell lines, are not considered fresh cells." The term "fresh" usually refers to primary cells that are prepared directly from the tissues of an organism and have not been subcultured. In light of the definition of "fresh cells" provided in the specification, Applicants submit that the term is not indefinite and request withdrawal of this rejection.

Rejections under 35 U.S.C. § 102(a)

Claims 51 and 59 were rejected under 35 U.S.C. § 102(a) as anticipated by Garver. Applicants respectfully traverse this rejection.

As amended, claim 51 recites a producer cell comprising 1) a first sequence encoding a replication defective retroviral vector comprising a genome lacking functional *env* and *gag-pol* genes, and a heterologous gene; and 2) "a set of DNA sequences" encoding *env* and *gag-pol*, wherein the DNA sequence encoding *env* is present on a separate construct to the DNA sequence encoding *gag-pol*. The second DNA sequence is in fact more than one sequence. Similarly, claim 59 recites the use of "a set of DNA sequences" encoding *env* and *gag-pol*, wherein the DNA sequence encoding *env* is present on a separate construct to the DNA sequence encoding *gag-pol*.

Thus, according to the claimed invention, at least three separate DNA constructs are introduced into a cell. The use of three separate DNA constructs is described in the application at page 8, lines 2-3. Introducing three separate DNA constructs reduces the likelihood of the constructs combining to form a replication competent retroviral vector.

In contrast to the claimed invention, Garver teaches transfection of two constructs. Moreover, the teachings of Garver would not enourage one of skill in the art to use more than two constructs. Garver presents the advantages of "coupling" the two constructs to increase transfection efficiency. Therefore, rather than suggesting the use of more constructs, Garver is suggesting that the use of less constructs is better, more efficient. Additionally, one of skill in the art would assume that it is better to have *env* and *gag-pol* on the same construct, to improve efficiency. Surprisingly, Applicants have discovered that this is not true. Transfection works equally well or better with three constructs, and, as discussed above, the risk of generating replication deficient virus is decreased.

Because Garver does not teach using a set of DNA sequences encoding *env* and *gag-pol*, wherein the DNA sequence encoding *env* is present on a separate construct to the sequence encoding *gag-pol*, nor does Garver suggest any advantages of using "a set of DNA sequences", Applicants respectfully request withdrawal of this rejection.

CONCLUSION

In view of the amendments and remarks presented herein, it is respectfully submitted that the application is in condition for allowance and notification to that effect is earnestly solicited. The Examiner is encouraged to contact Applicant's undersigned attorney to discuss this application if any questions should arise upon further examination of the pending claims.

Respectfully submitted,

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MARKED UP VERSION TO SHOW CHANGES MADE

Please amend the claims as shown below:

47. (AMENDED) A method for introducing a heterologous gene into a target cell in a subject, which comprises the following steps:

(i) conversion of a subject's cell into a producer cell, comprising introducing into the subject's cell:

a first DNA sequence encoding a replication defective retroviral vector, which comprises

(a) a defective retroviral genome lacking functional *env* and functional *gag-pol* genes; and

(b) the heterologous gene; and

a set of DNA sequences [second DNA sequence] encoding packaging components *env* and *gag-pol*, wherein the DNA sequence encoding *env* is present on a separate construct than the DNA sequence encoding *gag-pol*;

(ii) production of replication defective retroviral vector particles *in vivo* by the producer cell; and

(iii) virus-mediated delivery of the heterologous gene to the target cell *in vivo*.

51. (AMENDED) A producer cell comprising:

a first DNA sequence encoding a replication defective retroviral vector, which comprises

(i) a defective retroviral genome lacking functional *env* and functional *gag-pol* genes; and

(ii) at least one heterologous gene; and

a set of DNA sequences [second DNA sequence] encoding packaging components *env* and *gag-pol* wherein the DNA sequence encoding *env* is present on a separate construct than the DNA sequence encoding *gag-pol* which producer cell is a fresh cell from a subject.

[illegible] (AMENDED) A method of producing a replication defective retroviral vector in a subject, said vector comprising of at least one heterologous gene for delivery to a target cell within the

subject, which comprises the step of expressing the set of DNA sequences within a producer cell according to claim 54 within the subject.

59. (AMENDED) A method for making a producer cell *in vivo* in a subject comprising a step of introducing a set of DNA sequences into a cell within the subject, said set of DNA sequences comprising:

a first DNA sequence encoding replication defective retroviral vector, which comprises

(i) a defective retroviral genome lacking functional env and functional *gag-pol* genes; and

(ii) at least one heterologous gene; and

a set of DNA sequences [second DNA sequence] encoding packaging components env and *gag-pol* wherein the DNA sequence encoding env is present on a separate construct than the DNA sequence encoding *gag-pol*.

60. (AMENDED) A method or cell according to claim [1] 51, wherein the heterologous gene comprises at least one therapeutically active gene.

61. (AMENDED) A method or cell according to claim [1] 51, wherein said defective retroviral genome comprises any one or more of a primer binding site, integration sites and a packaging signal.